09/622101

REC'D 17 MAY 2000

WIPO PCT

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
B 3270 PCT		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP99/00945	12/02/1999	13/02/1998
International Patent Classification (IPC) or national classification and IPC C12P21/00		
Applicant MAX-PLANCK-GESELLSCHAFT ZUR FÖRDERUNG DER WISSENSC		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 7 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
10/09/1999	12.05.00
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Marie, A Telephone No. +49 89 2399 8413

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP99/00945

I. Basis of th r port

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-64 as originally filed

Claims, No.:

1-38 as received on 17/04/2000 with letter of 17/04/2000

Drawings, sheets:

1/7-7/7 as originally filed

2. The amendments have resulted in the cancellation of:

☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-22,24-38
	No:	Claims	23-23
Inventive step (IS)	Yes:	Claims	1-22,24-31,36,38
	No:	Claims	23-25,32-35,37
Industrial applicability (IA)	Yes:	Claims	1-38
	No:	Claims	

2. Citations and explanations

see separate sheet

1. As far as the priority right can be acknowledged, **Biochemistry, 1998, 37, 3677-3686** (**D1**) and **PNAS, 1998, 95, 14045-14050** (**D2**) cannot be taken into consideration, since they have been published after the priority date.

2. The problem underlying the failure of AZT is described in **Nature Medicine, 1997, 3/8, 836-837** (**D3**) and/or **Nature Structural Biology, 1997, 4/8, 601-604** (**D4**). In particular, the importance of the P-loop and the LID region is emphasised. Furthermore, the movement of the P-loop resulting in a 200-fold reduced phosphorylation rate of AZTMP in mentioned in **D4** on page 602.
D4 further suggests that 2 choices could be made to avoid said reduced phosphorylation rate and accumulation of toxic AZTMP, one of them is to modify TmpK (page 603).
However, none of these documents describes or suggests the solutions given in the present application. Therefore, basically the subject-matter of the present claims has to be considered novel (Article 33.2 PCT) and inventive (Article 33.3 PCT) over the cited prior art as fas as said claims are related to a polypeptide modified according to claim 1.

3.1 However, claim 23 embraces a composition containing only a non-modified nucleotide kinase, i.e. the item (a). Indeed, items (b)-(c) are either introduced with the adverb "...**optionally**..." or the preposition "...**or**...". Insofar they have no limitation affect and must not be present in the claimed composition.
Since, TmpK is described in both **D3** and **D4**, claims 23-25 cannot be considered as novel and/or inventive (Articles 33.2 and 33.3 PCT). This also applies to claim 37

3.2 An objection under Article 33.3 PCT can be raised against claims 32-35, 37 which also embrace *inter alia* the use of "...*Use of a prokaryotic protein having nucleoside or nucleotide kinase activity for a nucleoside or nucleotide analog...for the preparation of a pharmaceutical composition* ...", since said use is directly derivable from the known biological activity of said enzyme.

4. The formulation of claim 1 is not so clear (Article 6 PCT) because of the expression "...polypeptide *having or having an enhanced* kinase activity...".

5. Claims 32, 35 may give rise under certain patent laws to objections, since they can be considered as methods of treatment of the human body.